UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,730	05/08/2002	Dan L. Eaton	P3230R1C001-168	1384

30313 7590 09/17/2004

KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 MAIN STREET
IRVINE, CA 92614

EXAMINER	
SEHARASEYON, JEGATHEESAN	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,730	EATON ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/17/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice to comply, Appendix A1-5..

DETAILED ACTION

1. Applicant's preliminary amendment filed on 10 September 2002 is acknowledged and entered. Claims 1-20 are pending and under consideration. The claims are drawn to the nucleotide encoding the protein designated PRO1565, also identified as encoded by DNA737727-1673 and ATCC accession number 203459, shown in Figures 115 (nucleic acid) and 116 (protein).

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). Applicant is required to provide a paper copy of the CRF in response to the Office Action.

Information Disclosure Statement

4.The information disclosure statement, filed 9/17/2002 has no blast searches. Thus, the Examiner cannot determine the merits of the blast search results.

Priority Determination

5. The claimed nucleotide has no utility, see rejection below. Since no utility is disclosed in the priority applications and aren't enabling under 35 U.S.C. 112, as required under 119(e), no priority is granted. Accordingly, priority under 35 U.S.C. 120 is set at the instant filing date, 5/8/02.

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to the date recited above which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of, and fully enabled for, prior to that date.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8-10 and 15-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6a. The protein identified as PRO1565 (SEQ ID NO: 116) is not disclosed as being expressed on a cell surface. Accordingly, the limitation that the claimed protein comprises an "extracellular domain" (for example see claims 1, 6 and 14 parts (c) and (d)) is indefinite, as the art does not recognize soluble proteins as having such domains. Further, if the protein had an extracellular domain, the recitation of "the extracellular

domain", "lacking its associated signal sequence" (claim 1, 6 and 14, part (d), for example) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell. Claims 2-5, 8-10 and 15-20 are rejected insofar as they are depended on rejected claims 1, 6 and 14.

5b. Claims that recite that the claimed polynucleotide "hybridizes to" another sequence, such as claim 14, are indefinite as there is no limiting definition of such in the specification, and the metes and bounds of that which will hybridize are dependent upon the conditions under which the hybridization is performed. As the metes and bounds of what will hybridize to a given sequence are entirely dependent upon the conditions of hybridization and washing, the metes and bounds of the claims cannot be determined. With respect to claim 15, although the further limitation that the hybridization conditions are "stringent" is introduced, the term "stringent conditions" is also a relative term, and the metes and bounds of the claim cannot be determined. Claim 16 is rejected insofar as it is depended on rejected claim 14.

Rejections under 35 U.S.C. §101 and §112

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7a. Claims 1-20 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well-established utility.

Claims 1-20 are directed to isolated polynucleotides that are 80-100% identical to (a) a sequence encoding polypeptide of SEQ ID NO: 116 or (b) a sequence encoding the polypeptide of SEQ ID NO: 116 lacking signal sequence or (c) a sequence encoding the extracellular domain of SEQ ID NO: 116 or (d) a sequence encoding the extracellular domain of the polypeptide of SEQ ID NO: 116, lacking the signal sequence or (e) a polynucleotide sequence of SEQ ID NO: 115 or (f) a full-length coding sequence of SEQ ID NO: 115 or (g) the full-length coding sequence of the cDNA deposited under ATCC 203459. Dependent claims are directed to polynucleotides that hybridize to the above sequences, vectors and host cells comprising the isolated polynucleotides. The specification discloses the isolation of a polynucleotide sequence, SEQ ID NO: 115, which encodes a protein, SEQ ID NO: 116 which is disclosed as PRO1565 (see page 21). The specification contains numerous asserted utilities the claimed nucleotides, including use as a hybridization probe, in the generation of anti-sense RNA and DNA, "knock-out" animals, as a diagnostic tool, for therapeutic purposes and for the antibody production. Further, there is no disclosure that the protein encoded by the instant nucleotides is expected to be a transmembrane protein, nor of any extracellular domain. There is no biological activity, expression pattern, phenotype, disease or condition, ligand, binding partner, or any other specific feature that is disclosed as being associated with PRO1565 provided in the specification. In the instant invention, claims are directed to polynucleotide sequences encoding the polypeptide of SEQ ID NO: 116 (PRO1565).

The specification describes the polynucleotides encoding polypeptide PRO1565 that is an unspecified secreted transmembrane polypeptide. However, the art teaches that PRO1565 is a polypeptide that is similar to Chondromodulin like protein (see Appendix A1-A5). This family of proteins does not possess a common utility, but rather the proteins that can be broadly classified and have different activities, that confer different uses on them. Accordingly, the mere identification of a protein as belonging to a family, while indicative of evolutionary relatedness, is not indicative of function, nor by extension, of utility. The structure of the putative PRO1565 peptide is briefly discussed in Figure 116, as having putative transmembrane domains, corresponding to about amino acids 25-47. Potential signal peptide sequence is described around amino acids 1-40. In addition, Applicants also describe potential glycosaminoglycan attachment sites around amino acids 70-73, 85-88, 92-95, 133-136, 148-151, 192-195 and 239-242. Applicant has also described potential microbodies C-terminal targeting signal site at amino acids 315-317. Further, potential N-myristoylation site around amino acids 33-38, 95-100, 116-121, 215-220 and 272-277 has been described. The specification also describes a potential cytochrome C family heme-binding site signature at around amino acids 9-14. However, there is no functional characteristic associated with these motifs, hence the mere observation that they exist is not probative of function or utility. Further, there is no disclosure that the protein is expected to be a secreted protein, nor of any extracellular domain. There is no biological activity, expression pattern, phenotype, disease or condition, ligand, binding partner, any other specific feature that is disclosed as being associated with PRO1565. Without any information as to the specific

properties of PRO1565 or the polynucleotide encoding the same, the mere identification of such as having homology to a secreted transmembrane protein is not sufficient to impart any particular utility to the claimed polypeptides.

The specification discloses that PRO1565 tests positive in a single assay that stimulates the release of proteoglycans from cartilage tissue both basally and after stimulation with interleukin-1α (see page 138, Assay 97). In this assay the proteoglycan released from cartilage is measured by a colorimetric assay. Thus, it is claimed that PRO1565 polypeptide is useful for stimulating proteoglycan release from cartilage tissue. It is further stated this activity (for stimulating proteoglycan release from cartilage tissue) is useful for the "treatment of sports-related joint problems, articular cartilage defects, osteoarthritis or rheumatoid arthritis" (see page 138). This assay is not considered to impart utility to the protein PRO1565. The reason for this determination is that no results are presented, and the standard disclosed, "a positive result", is not considered to be an acceptable standard in the scientific community. It is well accepted in experimental science that, in order for a result to be positive, it must be *significantly* different from the control value, not "a positive result" as reported in the specification. In this case, it is unclear if the proteoglycan detected using the colorimetric assay, such that "a positive result" does not indicate anything more than that a trace amount of proteoglycan was present. Therefore, the assertion that the protein could be used in "treatment of sports-related joint problems, articular cartilage defects, osteoarthritis or rheumatoid arthritis" is not substantial. The Examiner further notes that he is unaware of *any* condition in which release of proteoglycan from the cartilage would be desirable,

even if, *in arguendo*, significant amounts of the proteoglycan was released from the cartilage upon the stimulation with PRO1565 protein. On the contrary, Lafeber et al. (1999) teach that preventing the cartilage destruction and the release of proteoglycan is necessary for protecting rheumatoid arthritis patients from joint destruction (abstract). In this study it was found apocynin (a plant derived compound) diminished the release of proteoglycans from the cartilage matrix, thus preventing joint destruction. Accordingly, the tacit assertion that PRO1565 stimulates proteoglycan release from cartilage does not meet the requirements of 35 U.S.C. § 101, as the assertion of utility would not be considered substantial by a person of ordinary skill in the art.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleotides encoding the polypeptides. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." Brenner v. Manson, 148 USPQ: at 696.

A substantial utility, by definition, is a utility the defines "real world" use, and a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not substantial utility. In the instant case, Applicant asserts that PRO1565 stimulates the release of proteoglycans from cartilage tissue both basally and after stimulation with interleukin-1α (if significant), at the most, is an interesting invitation for further research, experimentation and confirmation as to

whether the PRO1565 or the polynucleotide encoding is useful as a diagnosis marker, or suitable as a therapeutic target for treatment of diseases related to cartilage and joint problems. These further research and experimentation, however, is part of the act of invention, and until it has been undertaken, the claimed invention is not considered substantial.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8a. Claims 1-20 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above (Paragraph 7), one skilled in the art clearly would not know how to use the polynucleotide of SEQ ID NO: 115 nor polynucleotides 80, 85, 90, 95 or 99% identical to such, nor which encode a protein 80, 85, 90, 95 or 99% identical to the protein of SEQ ID NO: 116, nor polynucleotides which hybridize to any of the above.

Furthermore, even if a specific and substantial utility were subsequently established they would be enabled only for the polynucleotide of SEQ ID NO: 115 or fragments of such that are usable as hybridization probes and are not enabled for polynucleotides 80, 85, 90, 95 or 99% identical to such, nor which encode a protein 80, 85, 90, 95 or 99% identical to the protein of SEQ ID NO: 116, nor polynucleotides which

hybridize to any of the above because there is n no structural or functional information provided in the specification.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re *Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are directed to isolated polynucleotides having at least 80% identity to a SEQ ID NO: 115 or that encode the protein of SEQ ID NO: 116 with or without its signal peptide, or which encode the extracellular domain of SEQ ID NO: 116 with or without its signal peptide, or polynucleotides at least 80% identical to such encoding polynucleotides. Dependent claims are directed to polynucleotides that hybridize to the above sequences, vectors and host cells comprising the isolated polynucleotides. In the instant application, there is insufficient guidance regarding how to make PRO1565 polynucleotides variants recited in the claims.

The specification also is not enabling for the breadth of claims to polynucleotide molecules that hybridize to the disclosed sequences. It is noted that claims that recite hybridization language fail to provide adequate guidance, and do not recite that the polynucleotide encodes a protein, much less one having a specifically disclosed activity. First of all, it is pointed out that the term "hybridize" or "hybridization" generically refers to a process in which a strand of polynucleotide joins or matches up with a

complementary strand through the process of base pairing, wherein the process is basically used to locate or identify DNAs encoding specific proteins. It is well established in the art that 15-20 bases have been considered sufficient to achieve this process. The breadth of the claims includes polynucleotides of as little as 10 nucleotides. With these points in mind, it is the Examiner's position that giving the claims their broadest reasonable interpretation, this language reads on an infinite number of possible DNA sequences for which there is not sufficient enablement without undue experimentation because of the breath of claims, the lack of guidance provided and the quantity of experimentation needed to make or use the invention.

With respect to the hybridization use, as discussed above in paragraph 6 the invention lacks utility and thus lacks enablement. Even if utility were established, the enablement is commensurate in scope only with claims to polynucleotides that are fragments of SEQ ID NO: 115, said fragments of sufficient length to be used as hybridization probes or primers. However, enablement is *not* commensurate in scope with fragments of polynucleotides that differ from SEQ ID NO: 115 due to codon degeneracy, as it is not recognized in the art to use such sequences that are degenerate for such detection or synthesis, and the specification provides no guidance as to how or why to make such degenerate probes or primers. The specification also is not enabling for the breadth of claims to polynucleotide molecules that hybridize to the disclosed sequences because of the quantity of experimentation needed and the lack of guidance provided by the inventor.

The examples provided in the specification do not provide working examples of different DNA sequences that would enable a representative number of the above discussed DNA sequences with assurances that they can be used as probes or primers for the purpose of amplifying or detecting the PRO1565 gene. The mere recitation of this term, and the definitions provided do not serve as sufficient guidance to enable the breadth of the claims for the various DNA sequences claimed. See Ex parte *Forman*, 230 USPQ 546. Since the first paragraph of the statute under 35 U.S.C. 112 requires that there must be an enabling disclosure to support the breadth of the Claims, a review of the specification confirms that the scope of the various DNA sequences that are discussed above have not been enabled. There is but a single polynucleotide disclosed with reference to PRO1565, SEQ ID NO: 115. In the absence of working examples, breadth of claims and sufficient guidance, it would require undue experimentation to enable a commensurate number of the sequences that are encompassed by the claims.

Since the claimed polynucleotides are described at least in part in terms of the protein that might be encoded, the scope of the protein itself must be considered: The specification asserts that PRO1565 is an unspecified secreted and transmembrane polypeptide. However, this family of proteins does not possess a common utility, but rather the proteins that can be broadly classified and have different activities, that confer different uses on them. Accordingly, the mere identification of a protein as belonging to a family, while indicative of evolutionary relatedness, is not indicative of function, nor by extension, of utility. The structure of the putative PRO1565 peptide is briefly discussed in Figure 116, as having putative transmembrane domains, corresponding to about

amino acids 25-47. Potential signal peptide sequence is described around amino acids 1-40. In addition, Applicants also describe potential glycosaminoglycan attachment sites around amino acids 70-73, 85-88, 92-95, 133-136, 148-151, 192-195 and 239-242. Applicant has also described potential microbodies C-terminal targeting signal site at amino acids 315-317. Further, potential N-myristoylation site around amino acids 33-38, 95-100, 116-121, 215-220 and 272-277 has been described. The specification also describes a potential cytochrome C family heme-binding site signature at around amino acids 9-14.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Therefore, undue

experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope, i.e. all the polynucleotides with the various percent identities.

8b. Claims 1-5 and 15-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

The claims are drawn to polynucleotides having at least 80%, 85%, 95% or 99% sequence identity with a particular disclosed sequence, or that merely hybridize to a disclosed sequence. The claims do not require that the claimed polynucleotide encode a particular protein, nor that any protein encoded thereby possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. The specification teaches that PRO1565 has (unspecified) homology to secreted and transmembrane polypeptide. The structure of the putative PRO1565 peptide is briefly discussed in Figure 116, as having putative transmembrane domains, corresponding to about amino acids 25-47. Potential signal peptide sequence is described around amino acids 1-40. In addition, Applicants also describe potential

glycosaminoglycan attachment sites around amino acids 70-73, 85-88, 92-95, 133-136, 148-151, 192-195 and 239-242. Applicant has also described potential microbodies C-terminal targeting signal site at amino acids 315-317. Further, potential N-myristoylation site around amino acids 33-38, 95-100, 116-121, 215-220 and 272-277 has been described. The specification also describes a potential cytochrome C family heme-binding site signature at around amino acids 9-14. However, there is no functional characteristic associated with these motifs, hence the mere observation that they exist is not probative of function or utility. Further, there is no disclosure that the protein is expected to be a transmembrane protein, nor of any extracellular domain. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until

reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1616.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the human sequence.

Therefore, polynucleotides comprising the sequence set forth in SEQ ID NO: 115 or encoding the protein of SEQ ID NO: 116, or fragments thereof sufficiently long to be used as hybridization probes but not the full breadth of the claims meet the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless :
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9a. Claims 1-10 and 12-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Lok et al., (WO 00/29579) Pub date (5/2000).

Lok et al. describes full length cDNA sequences encoding amino acid sequence that has a 100% overall identity to SEQ ID NO: 116 (see Appendix A1). It also describes a protein sequence (SEQ ID NO: 2) that identical to SEQ ID NO: 116 (Appendix A4-A5). Thus, meeting the limitation of claims 1-7, 9, 12 and 13 of the instant invention. In addition, given this sequence identity the sequence of Lok et al., it would hybridize under stringent conditions (claims 14-16). Further, Lok et al. have described the expression of nucleotides containing vectors with promoter sequences in host cells (pages: 28-31). With respect to the limitation of "lacking its associated signal peptide" in claims 8 and 10 as Lok et al. teaches recombinant expression of the said polypeptide, the cDNA would produce the polypeptide identical to the present SEQ ID NO: 116, but lacking its associated signal peptide when transfected into the host cell. Thus, meeting the limitations of claims 8, 10, 17-20. Therefore, claims 1-20 are rejected as being anticipated by Lok et al., (WO 00/29579) Pub date (5/2000).

10. No claims are allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone

number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 09/04

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Notice to Comply	Application No.	Applicant(s)	
	10/063,730	Eaton et al.	
	Examiner	Art Unit	
	Seherasegun, J	1697	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☑ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

```
Db        667 CAGTGGGTGGTCCCTCAAGTGAAAGTAGAGAAGACCCGTCACGCCAGACAAGCAAGTGAG 726

Qy        241 GluGluLeuProIleAsnAspTyrThrGluAsnGlyIleGluPheAspProMetLeuAsp 260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        727 GAAGAACTTCCAATAAATGACTATACTGAAAATGGAATAGAATTTGATCCCATGCTGGAT 786

Qy        261 GluArgGlyTyrCysCysIleTyrCysArgArgGlyAsnArgTyrCysArgArgValCys 280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        787 GAGAGAGGTTATTGTTGTATTTACTGCCGTCGAGGCAACCGCTATTGCCGCCGCGTCTGT 846

Qy        281 GluProLeuLeuGlyTyrTyrProTyrProTyrCysTyrGlnGlyGlyArgValIleCys 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        847 GAACCTTTACTAGGCTACTACCCATATCCATACTGCTACCAAGGAGGACGAGTCATCTGT 906

Qy        301 ArgValIleMetProCysAsnTrpTrpValAlaArgMetLeuGlyArgVal 317
              |||||||||||||||||||||||||||||||||||||||||||||||||||
Db        907 CGTGTCATCATGCCTTGTAACTGGTGGGTGGCCCGCATGCTGGGGAGGGTC 957

RESULT 5
BD228713
LOCUS       BD228713                1178 bp    DNA     linear   PAT 17-JUL-2003
DEFINITION  Mammalian chondromodulin-like protein.
ACCESSION   BD228713
VERSION     BD228713.1  GI:33038483
KEYWORDS    JP 2002530078-A/1.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 1178)
  AUTHORS   Lok,S. and Presnell,S.R.
  TITLE     Mammalian chondromodulin-like protein
  JOURNAL   Patent: JP 2002530078-A 1 17-SEP-2002;
            ZYMOGENETICS INC
COMMENT     OS   Homo sapiens (human)
            PN   JP 2002530078-A/1
            PD   17-SEP-2002
            PF   12-NOV-1999 JP 2000582562
            PR   13-NOV-1998 US    09/191986
            PI   SI LOK,SCOTT R PRESNELL
            PC   C12N15/09,C07K14/51,C07K16/24,C12N15/00
            CC   Mammalian chondromodulin-like protein
            FH   Key             Location/Qualifiers
            FT   CDS             (58). .(1008).
FEATURES             Location/Qualifiers
     source          1. .1178
                     /organism="Homo sapiens"
                     /mol_type="genomic DNA"
                     /db_xref="taxon:9606"
ORIGIN

Alignment Scores:
Pred. No.:              5.17e-155      Length:         1178
Score:                  1745.00        Matches:        317
Percent Similarity:     100.00%        Conservative:   0
Best Local Similarity:  100.00%        Mismatches:     0
Query Match:            100.00%        Indels:         0
Db:                     6              Gaps:           0

US-10-063-730-116 (1-317) x BD228713 (1-1178)

Qy          1 MetAlaLysAsnProProGluAsnCysGluAspCysHisIleLeuAsnAlaGluAlaPhe 20
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         58 ATGGCAAAGAATCCTCCAGAGAATTGTGAAGACTGTCACATTCTAAATGCAGAAGCTTTT 117

Qy         21 LysSerLysLysIleCysLysSerLeuLysIleCysGlyLeuValPheGlyIleLeuAla 40
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        118 AAATCCAAGAAAATATGTAAATCACTTAAGATTTGTGGACTGGTGTTTGGTATCCTGGCC 177

Qy         41 LeuThrLeuIleValLeuPheTrpGlySerLysHisPheTrpProGluValProLysLys 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        178 CTAACTCTAATTGTCCTGTTTTGGGGGAGCAAGCACTTCTGGCCGGAGGTACCCAAAAAA 237

Qy         61 AlaTyrAspMetGluHisThrPheTyrSerAsnGlyGluLysLysIleTyrMetGlu 80
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        238 GCCTATGACATGGAGCACACTTTCTACAGCAATGGAGAGAAGAAGAAGATTTACATGGAA 297

Qy         81 IleAspProValThrArgThrGluIlePheArgSerGlyAsnGlyThrAspGluThrLeu 100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        298 ATTGATCCTGTGACCAGAACTGAAATATTCAGAAGCGGAAATGGCACTGATGAAACATTG 357

Qy        101 GluValHisAspPheLysAsnGlyTyrThrGlyIleTyrPheValGlyLeuGlnLysCys 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        358 GAAGTGCACGACTTTAAAAACGGATACACTGGCATCTACTTCGTGGGTCTTCAAAAATGT 417

Qy        121 PheIleLysThrGlnIleLysValIleProGluPheSerGluProGluGluGluIleAsp 140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        418 TTTATCAAAACTCAGATTAAAGTGATTCCTGAATTTTCTGAACCAGAAGAGGAAATAGAT 477

Qy        141 GluAsnGluGluIleThrThrThrPhePheGluGlnSerValIleTrpValProAlaGlu 160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        478 GAGAATGAAGAAATTACCACAACTTTCTTTGAACAGTCAGTGATTTGGGTCCCAGCAGAA 537

Qy        161 LysProIleGluAsnArgAspPheLeuLysAsnSerLysIleLeuGluIleCysAspAsn 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        538 AAGCCTATTGAAAACCGAGATTTTCTTAAAAATTCCAAAATTCTGGAGATTTGTGATAAC 597

Qy        181 ValThrMetTyrTrpIleAsnProThrLeuIleSerValSerGluLeuGlnAspPheGlu 200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        598 GTGACCATGTATTGGATCAATCCCACTCTAATATCAGTTTCTGAGTTACAAGACTTTGAG 657

Qy        201 GluGluGlyGluAspLeuHisPheProAlaAsnGluLysLysGlyIleGluGlnAsnGlu 220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        658 GAGGAGGGAGAAGATCTTCACTTTCCTGCCAACGAAAAAAAAGGGATTGAACAAAATGAA 717

Qy        221 GlnTrpValValProGlnValLysValGluLysThrArgHisAlaArgGlnAlaSerGlu 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        718 CAGTGGGTGGTCCCTCAAGTGAAAGTAGAGAAGACCCGTCACGCCAGACAAGCAAGTGAG 777

Qy        241 GluGluLeuProIleAsnAspTyrThrGluAsnGlyIleGluPheAspProMetLeuAsp 260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        778 GAAGAACTTCCAATAAATGACTATACTGAAAATGGAATAGAATTTGATCCCATGCTGGAT 837

Qy        261 GluArgGlyTyrCysCysIleTyrCysArgArgGlyAsnArgTyrCysArgArgValCys 280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        838 GAGAGAGGTTATTGTTGTATTTACTGCCGTCGAGGCAACCGCTATTGCCGCCGCGTCTGT 897

Qy        281 GluProLeuLeuGlyTyrTyrProTyrProTyrCysTyrGlnGlyGlyArgValIleCys 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        898 GAACCTTTACTAGGCTACTACCCATATCCATACTGCTACCAAGGAGGACGAGTCATCTGT 957

Qy        301 ArgValIleMetProCysAsnTrpTrpValAlaArgMetLeuGlyArgVal 317
              |||||||||||||||||||||||||||||||||||||||||||||||||||
Db        958 CGTGTCATCATGCCTTGTAACTGGTGGGTGGCCCGCATGCTGGGGAGGGTC 1008

RESULT 6
AF291656
LOCUS       AF291656                1184 bp    mRNA    linear   PRI 07-DEC-2001
DEFINITION  Homo sapiens chondromodulin-IB mRNA, complete cds.
ACCESSION   AF291656
VERSION     AF291656.1  GI:15077275
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 1184)
  AUTHORS   Brandau,O., Meindl,A., Fassler,R. and Aszodi,A.
  TITLE     A novel gene, tendin, is strongly expressed in tendons and
            ligaments and shows high homology with chondromodulin-I
  JOURNAL   Dev. Dyn. 221 (1), 72-80 (2001)
  MEDLINE   21255555
  PUBMED    11357195
REFERENCE   2  (bases 1 to 1184)
  AUTHORS   Brandau,O., Aszodi,A., Meindl,A. and Fassler,R.
  TITLE     Direct Submission
```

```
        Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
FERENCE 1  (bases 1 to 1200)
AUTHORS Yamana,K., Takahashi,Y., Wada,H. and Kasahara,Y.
ITLE    A novel polypeptide and its encoding gene
JOURNAL Patent: WO 0123557-A 1 05-APR-2001;
        TEIJIN LTD,KEI YAMANA,YUKIMI TAKAHASHI,HITOSHI WADA, YOSHINORI
        KASAHARA
MMENT   OS   Homo sapiens (human)
        PN   WO 0123557-A/1
        PD   05-APR-2001
        PF   29-SEP-2000 WO 2000JP006804
        PR   29-SEP-1999 JP 99P   275947
        PI   KEI YAMANA,YUKIMI TAKAHASHI,HITOSHI WADA,YOSHINORI KASAHARA PC
          C12N15/12,C12Q1/68,C12P21/08,C12N1/15,C12N1/19,C12N1/21,C12N5/ PC
          10
        CC
        FH   Key             Location/Qualifiers
        FT   CDS             (67). .(1020).
ATURES              Location/Qualifiers
   source           1. .1200
                    /organism="Homo sapiens"
                    /mol_type="genomic DNA"
                    /db_xref="taxon:9606"
IGIN

Query Match             99.2%;  Score 1187.2;  DB 6;  Length 1200;
Best Local Similarity   99.7%;  Pred. No. 1.1e-283;
Matches 1189;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

          1 CAGCAGTGGTCTCTCAGTCCTCTCAAAGCAAGGAAAGAGTACTGTGTGCTGAGAGACCAT 60
            ||||||  ||||||||||||||||||||||||||||||||||||||||||||||||||||
          9 CAGCAGGTGTCTCTCAGTCCTCTCAAAGCAAGGAAAGAGTACTGTGTGCTGAGAGACCAT 68

         61 GGCAAAGAATCCTCCAGAGAATTGTGAAGACTGTCACATTCTAAATGCAGAAGCTTTTAA 120
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
         69 GGCAAAGAATCCTCCAGAGAATTGTGAAGACTGTCACATTCTAAATGCAGAAGCTTTTAA 128

        121 ATCCAAGAAAATATGTAAATCACTTAAGATTTGTGGACTGGTGTTTGGTATCCTGGCCCT 180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        129 ATCCAAGAAAATATGTAAATCACTTAAGATTTGTGGACTGGTGTTTGGTATCCTGGCCCT 188

        181 AACTCTAATTGTCCTGTTTTGGGGGAGCAAGCACTTCTGGCCGGAGGTACCCAAAAAAGC 240
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        189 AACTCTAATTGTCCTGTTTTGGGGGAGCAAGCACTTCTGGCCGGAGGTACCCAAAAAAGC 248

        241 CTATGACATGGAGCACACTTTCTACAGCAATGGAGAGAAGAAGAAGATTTACATGGAAAT 300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        249 CTATGACATGGAGCACACTTTCTACAGCAATGGAGAGAAGAAGAAGATTTACATGGAAAT 308

        301 TGATCCTGTGACCAGAACTGAAATATTCAGAAGCGGAAATGGCACTGATGAAACATTGGA 360
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        309 TGATCCTGTGACCAGAACTGAAATATTCAGAAGCGGAAATGGCACTGATGAAACATTGGA 368

        361 AGTGCACGACTTTAAAAACGGATACACTGGCATCTACTTCGTGGGTCTTCAAAAATGTTT 420
            ||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        369 AGTACACGACTTTAAAAACGGATACACTGGCATCTACTTCGTGGGTCTTCAAAAATGTTT 428

        421 TATCAAAACTCAGATTAAAGTGATTCCTGAATTTTCTGAACCAGAAGAGGAAATAGATGA 480
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        429 TATCAAAACTCAGATTAAAGTGATTCCTGAATTTTCTGAACCAGAAGAGGAAATAGATGA 488

        481 GAATGAAGAAATTACCACAACTTTCTTTGAACAGTCAGTGATTTGGGTCCCAGCAGAAAA 540
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        489 GAATGAAGAAATTACCACAACTTTCTTTGAACAGTCAGTGATTTGGGTCCCAGCAGAAAA 548

        541 GCCTATTGAAAACCGAGATTTTCTTAAAAATTCCAAAATTCTGGAGATTTGTGATAACGT 600
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        549 GCCTATTGAAAACCGAGATTTTCTTAAAAATTCCAAAATTCTGGAGATTTGTGATAACGT 608

        601 GACCATGTATTGGATCAATCCCACTCTAATATCAGTTTCTGAGTTACAAGACTTTGAGGA 660
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
        609 GACCATGTATTGGATCAATCCCACTCTAATATCAGTTTCTGAGTTACAAGACTTTGAGGA 668

Qy      661 GGAGGGAGAAGATCTTCACTTTCCTGCCAACGAAAAAAAAGGGATTGAACAAAATGAACA 720
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      669 GGAGGGAGAAGATCTTCACTTTCCTGCCAACGAAAAAAAAGGGATTGAACAAAATGAACA 728

Qy      721 GTGGGTGGTCCCTCAAGTGAAAGTAGAGAAGACCCGTCACGCCAGACAAGCAAGTGAGGA 780
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      729 GTGGGTGGTCCCTCAAGTGAAAGTAGAGAAGACCCGTCACGCCAGACAAGCAAGTGAGGA 788

Qy      781 AGAACTTCCAATAAATGACTATACTGAAAATGGAATAGAATTTGATCCCATGCTGGATGA 840
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      789 AGAACTTCCAATAAATGACTATACTGAAAATGGAATAGAATTTGATCCCATGCTGGATGA 848

Qy      841 GAGAGGTTATTGTTGTATTTACTGCCGTCGAGGCAACCGCTATTGCCGCCGCGTCTGTGA 900
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      849 GAGAGGTTATTGTTGTATTTACTGCCGTCGAGGCAACCGCTATTGCCGCCGCGTCTGTGA 908

Qy      901 ACCTTTACTAGGCTACTACCCATATCCATACTGCTACCAAGGAGGACGAGTCATCTGTCG 960
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      909 ACCTTTACTAGGCTACTACCCATATCCATACTGCTACCAAGGAGGACGAGTCATCTGTCG 968

Qy      961 TGTCATCATGCCTTGTAACTGGTGGGTGGCCCGCATGCTGGGGAGGGTCTAATAGGAGGT 1020
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      969 TGTCATCATGCCTTGTAACTGGTGGGTGGCCCGCATGCTGGGGAGGGTCTAATAGGAGGT 1028

Qy     1021 TTGAGCTCAAATGCTTAAACTGCTGGCAACATATAATAAATGCATGCTATTCAATGAATT 1080
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1029 TTGAGCTCAAATGCTTAAACTGCTGGCAACATATAATAAATGCATGCTATTCAATGAATT 1088

Qy     1081 TCTGCCTATGAGGCATCTGGCCCCTGGTAGCCAGCTCTCCAGAATTACTTGTAGGTAATT 1140
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1089 TCTGCCTATGAGGCATCTGGCCCCTGGTAGCCAGCTCTCCAGAATTACTTGTAGGTAATT 1148

Qy     1141 CCTCTCTTCATGTTCTAATAAACTTCTACATTATCACCAAAAAAAAAAAAAA 1192
            ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1149 CCTCTCTTCATGTTCTAATAAACTTCTACATTATCACCAAAAAAAAAAAAAA 1200
```

```
RESULT 8
BD228713
LOCUS       BD228713                1178 bp    DNA     linear   PAT 17-JUL-2003
DEFINITION  Mammalian chondromodulin-like protein.
ACCESSION   BD228713
VERSION     BD228713.1  GI:33038483
KEYWORDS    JP 2002530078-A/1.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 1178)
  AUTHORS   Lok,S. and Presnell,S.R.
  TITLE     Mammalian chondromodulin-like protein
  JOURNAL   Patent: JP 2002530078-A 1 17-SEP-2002;
            ZYMOGENETICS INC
COMMENT     OS   Homo sapiens (human)
            PN   JP 2002530078-A/1
            PD   17-SEP-2002
            PF   12-NOV-1999 JP 2000582562
            PR   13-NOV-1998 US    09/191986
            PI   SI-LOK,SCOTT R PRESNELL
            PC   C12N15/09,C07K14/51,C07K16/24,C12N15/00
            CC   Mammalian chondromodulin-like protein
            FH   Key             Location/Qualifiers
            FT   CDS             (58). .(1008).
FEATURES             Location/Qualifiers
     source          1. .1178
                     /organism="Homo sapiens"
                     /mol_type="genomic DNA"
                     /db_xref="taxon:9606"
ORIGIN

  Query Match             98.4%;  Score 1178;  DB 6;  Length 1178;
  Best Local Similarity   100.0%;  Pred. No. 2.2e-281;
  Matches 1178;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;
```

```
Qy          2 AGCAGTGGTCTCTCAGTCCTCTCAAAGCAAGGAAAGAGTACTGTGTGCTGAGAGACCATG 61
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 AGCAGTGGTCTCTCAGTCCTCTCAAAGCAAGGAAAGAGTACTGTGTGCTGAGAGACCATG 60

Qy         62 GCAAAGAATCCTCCAGAGAATTGTGAAGACTGTCACATTCTAAATGCAGAAGCTTTTAAA 121
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GCAAAGAATCCTCCAGAGAATTGTGAAGACTGTCACATTCTAAATGCAGAAGCTTTTAAA 120

Qy        122 TCCAAGAAAATATGTAAATCACTTAAGATTTGTGGACTGGTGTTTGGTATCCTGGCCCTA 181
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 TCCAAGAAAATATGTAAATCACTTAAGATTTGTGGACTGGTGTTTGGTATCCTGGCCCTA 180

Qy        182 ACTCTAATTGTCCTGTTTTGGGGGAGCAAGCACTTCTGGCCGGAGGTACCCAAAAAAGCC 241
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 ACTCTAATTGTCCTGTTTTGGGGGAGCAAGCACTTCTGGCCGGAGGTACCCAAAAAAGCC 240

Qy        242 TATGACATGGAGCACACTTTCTACAGCAATGGAGAGAAGAAGAAGATTTACATGGAAATT 301
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 TATGACATGGAGCACACTTTCTACAGCAATGGAGAGAAGAAGAAGATTTACATGGAAATT 300

Qy        302 GATCCTGTGACCAGAACTGAAATATTCAGAAGCGGAAATGGCACTGATGAAACATTGGAA 361
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 GATCCTGTGACCAGAACTGAAATATTCAGAAGCGGAAATGGCACTGATGAAACATTGGAA 360

Qy        362 GTGCACGACTTTAAAAACGGATACACTGGCATCTACTTCGTGGGTCTTCAAAAATGTTTT 421
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 GTGCACGACTTTAAAAACGGATACACTGGCATCTACTTCGTGGGTCTTCAAAAATGTTTT 420

Qy        422 ATCAAAACTCAGATTAAAGTGATTCCTGAATTTTCTGAACCAGAAGAGGAAATAGATGAG 481
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 ATCAAAACTCAGATTAAAGTGATTCCTGAATTTTCTGAACCAGAAGAGGAAATAGATGAG 480

Qy        482 AATGAAGAAATTACCACAACTTTCTTTGAACAGTCAGTGATTTGGGTCCCAGCAGAAAAG 541
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 AATGAAGAAATTACCACAACTTTCTTTGAACAGTCAGTGATTTGGGTCCCAGCAGAAAAG 540

Qy        542 CCTATTGAAAACCGAGATTTTCTTAAAAATTCCAAAATTCTGGAGATTTGTGATAACGTG 601
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 CCTATTGAAAACCGAGATTTTCTTAAAAATTCCAAAATTCTGGAGATTTGTGATAACGTG 600

Qy        602 ACCATGTATTGGATCAATCCCACTCTAATATCAGTTTCTGAGTTACAAGACTTTGAGGAG 661
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ACCATGTATTGGATCAATCCCACTCTAATATCAGTTTCTGAGTTACAAGACTTTGAGGAG 660

Qy        662 GAGGGAGAAGATCTTCACTTTCCTGCCAACGAAAAAAAAGGGATTGAACAAAATGAACAG 721
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 GAGGGAGAAGATCTTCACTTTCCTGCCAACGAAAAAAAAGGGATTGAACAAAATGAACAG 720

Qy        722 TGGGTGGTCCCTCAAGTGAAAGTAGAGAAGACCCGTCACGCCAGACAAGCAAGTGAGGAA 781
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 TGGGTGGTCCCTCAAGTGAAAGTAGAGAAGACCCGTCACGCCAGACAAGCAAGTGAGGAA 780

Qy        782 GAACTTCCAATAAATGACTATACTGAAAATGGAATAGAATTTGATCCCATGCTGGATGAG 841
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 GAACTTCCAATAAATGACTATACTGAAAATGGAATAGAATTTGATCCCATGCTGGATGAG 840

Qy        842 AGAGGTTATTGTTGTATTTACTGCCGTCGAGGCAACCGCTATTGCCGCCGCGTCTGTGAA 901
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 AGAGGTTATTGTTGTATTTACTGCCGTCGAGGCAACCGCTATTGCCGCCGCGTCTGTGAA 900

Qy        902 CCTTTACTAGGCTACTACCCATATCCATACTGCTACCAAGGAGGACGAGTCATCTGTCGT 961
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 CCTTTACTAGGCTACTACCCATATCCATACTGCTACCAAGGAGGACGAGTCATCTGTCGT 960

Qy        962 GTCATCATGCCTTGTAACTGGTGGGTGGCCCGCATGCTGGGGAGGGTCTAATAGGAGGTT 1021
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 GTCATCATGCCTTGTAACTGGTGGGTGGCCCGCATGCTGGGGAGGGTCTAATAGGAGGTT 1020

Qy       1022 TGAGCTCAAATGCTTAAACTGCTGGCAACATATAATAAATGCATGCTATTCAATGAATTT 1081
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 TGAGCTCAAATGCTTAAACTGCTGGCAACATATAATAAATGCATGCTATTCAATGAATTT 1080
```

```
Qy       1082 CTGCCTATGAGGCATCTGGCCCCTGGTAGCCAGCTCTCCAGAATTACTTGTAGGTAATTC 1141
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 CTGCCTATGAGGCATCTGGCCCCTGGTAGCCAGCTCTCCAGAATTACTTGTAGGTAATTC 1140

Qy       1142 CTCTCTTCATGTTCTAATAAACTTCTACATTATCACCA 1179
              |||||||||||||||||||||||||||||||||||||
Db       1141 CTCTCTTCATGTTCTAATAAACTTCTACATTATCACCA 1178


RESULT 9
AR338896
LOCUS       AR338896                1380 bp    DNA     linear   PAT 17-AUG-2003
DEFINITION  Sequence 387 from patent US 6569662.
ACCESSION   AR338896
VERSION     AR338896.1  GI:33725753
KEYWORDS    .
SOURCE      Unknown.
  ORGANISM  Unknown.
            Unclassified.
REFERENCE   1  (bases 1 to 1380)
  AUTHORS   Tang,Y.T., Zhou,P. and Drmanac,R.T.
  TITLE     Nucleic acids and polypeptides
  JOURNAL   Patent: US 6569662-A 387 27-MAY-2003;
FEATURES             Location/Qualifiers
     source          1. .1380
                     /organism="unknown"
                     /mol_type="genomic DNA"
ORIGIN

  Query Match           98.1%;  Score 1174;  DB 6;  Length 1380;
  Best Local Similarity   99.6%;  Pred. No. 2.1e-280;
  Matches 1177;  Conservative    0;  Mismatches    5;  Indels    0;  Gaps    0;

Qy          1 CAGCAGTGGTCTCTCAGTCCTCTCAAAGCAAGGAAAGAGTACTGTGTGCTGAGAGACCAT 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         73 CAGCAGGGGTCTCTCAGTCCTCTCAAAGCAAGGAAAGAGTACTGTGTGCTGAGAGACCAT 132

Qy         61 GGCAAAGAATCCTCCAGAGAATTGTGAAGACTGTCACATTCTAAATGCAGAAGCTTTTAA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        133 GGCAAAGAATGGTCCAGAGAATTGTGAAGACTGTCACATTCTAAATGCAGAAGCTTTTAA 192

Qy        121 ATCCAAGAAAATATGTAAATCACTTAAGATTTGTGGACTGGTGTTTGGTATCCTGGCCCT 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        193 ATCCAAGAAAATATGTAAATCACTTAAGATTTGTGGACTGGTGTTTGGTATCCTGGCCCT 252

Qy        181 AACTCTAATTGTCCTGTTTTGGGGGAGCAAGCACTTCTGGCCGGAGGTACCCAAAAAAGC 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        253 AACTCTAATTGTCCTGTTTTGGGGGAGCAAGCACTTCTGGCCGGAGGTACCCAAAAAAGC 312

Qy        241 CTATGACATGGAGCACACTTTCTACAGCAATGGAGAGAAGAAGAAGATTTACATGGAAAT 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        313 CTATGACATGGAGCACACTTTCTACAGCAATGGAGAGAAGAAGAAGATTTACATGGAAAT 372

Qy        301 TGATCCTGTGACCAGAACTGAAATATTCAGAAGCGGAAATGGCACTGATGAAACATTGGA 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        373 TGATCCTGTGACCAGAACTGAAATATTCAGAAGCGGAAATGGCACTGATGAAACATTGGA 432

Qy        361 AGTGCACGACTTTAAAAACGGATACACTGGCATCTACTTCGTGGGTCTTCAAAAATGTTT 420
              ||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        433 AGTACACGACTTTAAAAACGGATACACTGGCATCTACTTCGTGGGTCTTCAAAAATGTTT 492

Qy        421 TATCAAAACTCAGATTAAAGTGATTCCTGAATTTTCTGAACCAGAAGAGGAAATAGATGA 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        493 TATCAAAACTCAGATTAAAGTGATTCCTGAATTTTCTGAACCAGAAGAGGAAATAGATGA 552

Qy        481 GAATGAAGAAATTACCACAACTTTCTTTGAACAGTCAGTGATTTGGGTCCCAGCAGAAAA 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        553 GAATGAAGAAATTACCACAACTTTCTTTGAACAGTCAGTGATTTGGGTCCCAGCAGAAAA 612

Qy        541 GCCTATTGAAAACCGAGATTTTCTTAAAAATTCCAAAATTCTGGAGATTTGTGATAACGT 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        613 GCCTATTGAAAACCGAGATTTTCTTAAAAATTCCAAAATTCTGGAGATTTGTGATAACGT 672
```

GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: September 7, 2004, 19:01:28 ; Search time 126 Seconds
(without alignments)
710.854 Million cell updates/sec

Title: US-10-063-730-116
Perfect score: 1745
Sequence: 1 MAKNPPENCEDCHILNAEAF.....VICRVIMPCNWWVARMLGRV 317

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 1586107 seqs, 282547505 residues

Total number of hits satisfying chosen parameters: 1586107

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_29Jan04:*
1: geneseqp1980s:*
2: geneseqp1990s:*
3: geneseqp2000s:*
4: geneseqp2001s:*
5: geneseqp2002s:*
6: geneseqp2003as:*
7: geneseqp2003bs:*
8: geneseqp2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	1745	100.0	317	3	AAY71262	Aay71262 Human cho
2	1745	100.0	317	3	AAY99430	Aay99430 Human PRO
3	1745	100.0	317	3	AAB25665	Aab25665 Human sec
4	1745	100.0	317	4	AAB66179	Aab66179 Protein o
5	1745	100.0	317	4	AAB96985	Aab96985 Human ang
6	1745	100.0	317	4	AAU12433	Aau12433 Human PRO
7	1745	100.0	317	4	AAB87583	Aab87583 Human PRO
8	1745	100.0	317	4	AAB99936	Aab99936 Human new
9	1745	100.0	317	4	AAB82755	Aab82755 Human cho
10	1745	100.0	317	5	ABG95908	Abg95908 Human sec
11	1745	100.0	317	6	ABO17877	Abo17877 Novel hum
12	1745	100.0	317	6	ABU81131	Abu81131 Human PRO
13	1745	100.0	317	6	ABU90933	Abu90933 Novel hum
14	1745	100.0	317	6	ABO33992	Abo33992 Human sec
15	1745	100.0	317	6	ABU72009	Abu72009 Novel hum
16	1745	100.0	317	6	ABU66831	Abu66831 Human PRO
17	1745	100.0	317	6	ABU71563	Abu71563 Human sec
18	1745	100.0	317	6	ABU59912	Abu59912 Novel sec
19	1745	100.0	317	6	ABU72344	Abu72344 Human PRO
20	1745	100.0	317	6	ABU91017	Abu91017 Human PRO
21	1745	100.0	317	6	ABO27338	Abo27338 Human sec
22	1745	100.0	317	6	ABO25102	Abo25102 Human sec
23	1745	100.0	317	6	ABU92533	Abu92533 Human sec
24	1745	100.0	317	6	ABU81203	Abu81203 Human sec
25	1745	100.0	317	6	ABO53317	Abo53317 Novel hum
26	1745	100.0	317	6	ABU67107	Abu67107 Human sec
27	1745	100.0	317	6	ABU98320	Abu98320 Novel hum
28	1745	100.0	317	6	ABU89325	Abu89325 Novel hum
29	1745	100.0	317	6	ABU82532	Abu82532 Novel hum
30	1745	100.0	317	6	ABU96496	Abu96496 Human PRO
31	1745	100.0	317	6	ABU72166	Abu72166 Human PRO
32	1745	100.0	317	6	ADA46043	Ada46043 Novel hum
33	1745	100.0	317	6	ADA76474	Ada76474 Human PRO
34	1745	100.0	317	6	ADB17173	Adb17173 Human tra
35	1745	100.0	317	6	ADA19124	Ada19124 Human PRO
36	1745	100.0	317	6	ADA61747	Ada61747 Homo sapi
37	1745	100.0	317	6	ADB19532	Adb19532 Novel hum
38	1745	100.0	317	6	ADB28073	Adb28073 Human PRO
39	1745	100.0	317	6	ADA86552	Ada86552 Novel hum
40	1745	100.0	317	6	ADB16116	Adb16116 Human PRO
41	1745	100.0	317	6	ADA47902	Ada47902 Human PRO
42	1745	100.0	317	6	ABO44296	Abo44296 Human sec
43	1745	100.0	317	6	ABO33672	Abo33672 Novel hum
44	1745	100.0	317	6	ADA19978	Ada19978 Novel hum
45	1745	100.0	317	6	ADA67697	Ada67697 Human PRO

ALIGNMENTS

RESULT 1
AAY71262
ID AAY71262 standard; protein; 317 AA.
XX
AC AAY71262;
XX
DT 21-SEP-2000 (first entry)
XX
DE Human chondromodulin-like protein, Zchm1.
XX
KW Chondromodulin-like protein; Zchm1; human; chromosome 11p15.4; cancer;
KW cell differentiation regulator; osteoblast proliferation stimulator;
KW cytostatic; diagnostic; therapeutic; polypeptide-toxin fusion protein;
KW class II cell surface protein; transmembrane domain; gene therapy;
KW targeted cell inhibition.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Domain 31. .50
FT /label= Transmembrane_domain
FT /note= "Alternative amino-terminal hydrophobic sequence"
FT Domain 34. .48
FT /label= Transmembrane_domain
FT /note= "Amino-terminal hydrophobic sequence"
FT Protein 48. .311
FT /note= "Mature soluble form of chondromodulin-like
FT protein, Zchm1-1"
FT Protein 202. .311
FT /note= "Mature soluble form of chondromodulin-like
FT protein, Zchm1-2"
FT Cleavage-site 213. .214
FT /label= Dibasic_cleavage_site
FT /note= "Alternative cleavage site as stated in page 13 of
FT the specification"
FT Cleavage-site 214. .215
FT /note= "Conserved site of cleavage that produces mature
FT Zchm1 protein"
FT Protein 215. .317
FT /note= "Mature chondromodulin-like protein, Zchm1-1"
FT Protein 255. .317
FT /note= "Mature chondromodulin-like protein, Zchm1-2"
FT Domain 255. .316
FT /label= Carboxyl_terminal_domain
FT /note= "Has sequence identity to bovine and human
FT chondromodulin-I (Chm-I)"
XX
PN WO200029579-A1.

Applicant's Copy

Appendix A5

XX
PD 25-MAY-2000.
XX
PF 12-NOV-1999; 99WO-US026909.
XX
PR 13-NOV-1998; 98US-00191986.
XX
PA (ZYMO) ZYMOGENETICS INC.
XX
PI Lok S, Presnell SR;
XX
DR WPI; 2000-387792/33.
DR N-PSDB; AAD01066.
XX
PT Polynucleotide encoding mammalian chondromodulin-like polypeptide useful
PT for gene therapy of various disorders by regulating growth or
PT differentiation of cells especially cancer cells.
XX
PS Claim 2; Page 77-78; 87pp; English.
XX
CC The present sequence is the human chondromodulin-like protein, Zchm1. The
CC presence of an amino-terminal hydrophobic transmembrane domain, is a
CC structural feature of class II cell surface proteins. Zchm1 may be
CC anchored on the cell membrane, via its transmembrane domain. It has
CC sequence homology to bovine and human Chm-I. The Zchm1 locus is mapped to
CC chromosome 11p15.4. It functions as a cell differentiation regulator and
CC osteoblast proliferation stimulator. Zchm1 can be used as growth or
CC differentiation regulator for cells, especially the mesenchymal,
CC myogenic, chondrogenic or endothelial cells. Zchm1 proteins or antibodies
CC are useful for identifying or treating tissues or organs expressing the
CC anti-complementary molecule, e.g., receptor or antigen. The Zchm1
CC polypeptides conjugated to drugs, toxins, radionuclides are useful for in
CC vivo diagnostic or therapeutic applications and polypeptide-toxin fusion
CC proteins are useful for targeted cell or tissue inhibition or ablation
CC for treating various disorders, especially cancer. It is useful for gene
CC therapy of disorders associated with altered Zchm1 activity
XX
SQ Sequence 317 AA;

Query Match 100.0%; Score 1745; DB 3; Length 317;
Best Local Similarity 100.0%; Pred. No. 6.6e-153;
Matches 317; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 MAKNPPENCEDCHILNAEAFKSKKICKSLKICGLVFGILALTLIVLFWGSKHFWPEVPKK 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MAKNPPENCEDCHILNAEAFKSKKICKSLKICGLVFGILALTLIVLFWGSKHFWPEVPKK 60

Qy         61 AYDMEHTFYSNGEKKKIYMEIDPVTRTEIFRSGNGTDETLEVHDFKNGYTGIYFVGLQKC 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 AYDMEHTFYSNGEKKKIYMEIDPVTRTEIFRSGNGTDETLEVHDFKNGYTGIYFVGLQKC 120

Qy        121 FIKTQIKVIPEFSEPEEEIDENEEITTTFFEQSVIWVPAEKPIENRDFLKNSKILEICDN 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 FIKTQIKVIPEFSEPEEEIDENEEITTTFFEQSVIWVPAEKPIENRDFLKNSKILEICDN 180

Qy        181 VTMYWINPTLISVSELQDFEEEGEDLHFPANEKKGIEQNEQWVVPQVKVEKTRHARQASE 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VTMYWINPTLISVSELQDFEEEGEDLHFPANEKKGIEQNEQWVVPQVKVEKTRHARQASE 240

Qy        241 EELPINDYTENGIEFDPMLDERGYCCIYCRRGNRYCRRVCEPLLGYYPYPYCYQGGRVIC 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 EELPINDYTENGIEFDPMLDERGYCCIYCRRGNRYCRRVCEPLLGYYPYPYCYQGGRVIC 300

Qy        301 RVIMPCNWWVARMLGRV 317
              |||||||||||||||||
Db        301 RVIMPCNWWVARMLGRV 317
```

RESULT 2
AAY99430
ID AAY99430 standard; protein; 317 AA.
XX
AC AAY99430;

XX
DT 08-AUG-2000 (first entry)
XX
DE Human PRO1565 (UNQ771) amino acid sequence SEQ ID NO:322.
XX
KW Human; PRO polypeptide; membrane bound protein; receptor; diagnosis;
KW transmembrane; secretion; immunoadhesion; pharmaceutical; screening.
XX
OS Homo sapiens.
XX
PN WO200012708-A2.
XX
PD 09-MAR-2000.
XX
PF 01-SEP-1999; 99WO-US020111.
XX
PR 01-SEP-1998; 98US-0098716P.
PR 01-SEP-1998; 98US-0098749P.
PR 01-SEP-1998; 98US-0098750P.
PR 02-SEP-1998; 98US-0098803P.
PR 02-SEP-1998; 98US-0098821P.
PR 02-SEP-1998; 98US-0098843P.
PR 09-SEP-1998; 98US-0099536P.
PR 09-SEP-1998; 98US-0099596P.
PR 09-SEP-1998; 98US-0099598P.
PR 09-SEP-1998; 98US-0099602P.
PR 09-SEP-1998; 98US-0099642P.
PR 10-SEP-1998; 98US-0099741P.
PR 10-SEP-1998; 98US-0099754P.
PR 10-SEP-1998; 98US-0099763P.
PR 10-SEP-1998; 98US-0099792P.
PR 10-SEP-1998; 98US-0099808P.
PR 10-SEP-1998; 98US-0099812P.
PR 10-SEP-1998; 98US-0099815P.
PR 10-SEP-1998; 98US-0099816P.
PR 15-SEP-1998; 98US-0100385P.
PR 15-SEP-1998; 98US-0100388P.
PR 15-SEP-1998; 98US-0100390P.
PR 16-SEP-1998; 98US-0100584P.
PR 16-SEP-1998; 98US-0100627P.
PR 16-SEP-1998; 98US-0100661P.
PR 16-SEP-1998; 98US-0100662P.
PR 16-SEP-1998; 98US-0100664P.
PR 17-SEP-1998; 98US-0100683P.
PR 17-SEP-1998; 98US-0100684P.
PR 17-SEP-1998; 98US-0100710P.
PR 17-SEP-1998; 98US-0100711P.
PR 17-SEP-1998; 98US-0100919P.
PR 17-SEP-1998; 98US-0100930P.
PR 18-SEP-1998; 98US-0100848P.
PR 18-SEP-1998; 98US-0100849P.
PR 18-SEP-1998; 98US-0101014P.
PR 18-SEP-1998; 98US-0101068P.
PR 18-SEP-1998; 98US-0101071P.
PR 22-SEP-1998; 98US-0101279P.
PR 23-SEP-1998; 98US-0101471P.
PR 23-SEP-1998; 98US-0101472P.
PR 23-SEP-1998; 98US-0101474P.
PR 23-SEP-1998; 98US-0101475P.
PR 23-SEP-1998; 98US-0101476P.
PR 23-SEP-1998; 98US-0101477P.
PR 23-SEP-1998; 98US-0101479P.
PR 24-SEP-1998; 98US-0101738P.
PR 24-SEP-1998; 98US-0101741P.
PR 24-SEP-1998; 98US-0101743P.
PR 24-SEP-1998; 98US-0101915P.
PR 24-SEP-1998; 98US-0101916P.
PR 29-SEP-1998; 98US-0102207P.
PR 29-SEP-1998; 98US-0102240P.
PR 29-SEP-1998; 98US-0102307P.
PR 29-SEP-1998; 98US-0102330P.
PR 29-SEP-1998; 98US-0102331P.
PR 30-SEP-1998; 98US-0102484P.